# News and Views

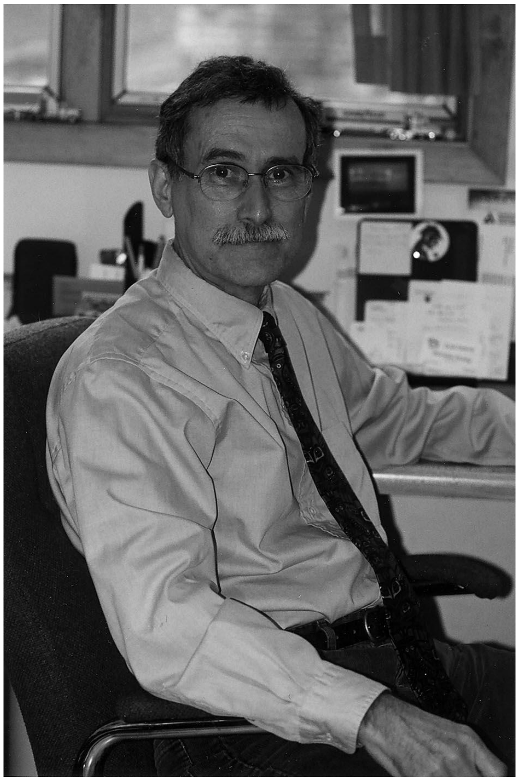
## A View on the Science: Physical Anthropology at the Millennium

KENNETH M. WEISS

*Department of Anthropolohy*

*The Pennsylvania State University*

*University Park, PA 16802*



Kenneth M. Weiss is past Head of the Department of Anthropology at the Pennsylvania State University. He holds the title of Distinguished Professor, and in 1993 received the Faculty Scholars Medal, Life and Heatlh Sciences, from Penn State University. In 1972 he was the recipient of the Juan Comas Prize of the American Association of Physical Anthropologists. Dr. Weiss is regarded as a leading theoretician of the biomedical sciences for his integrative approach which links demography, development, epidemiology, evolution and molecular genetics.

*EDITOR's NOTE* The year 2000 marks the onset of the 21rst century. Physical anthropologists will provide brief reflections on our discipline, including what attracted them to it, and their views on the directions our discipline may pursue as we enter, in January 2001, the third millennium. Am J Phys Anthropol 111:295–299, 2000.


I entered anthropology in the middle of a remarkable century of discovery in biology. My undergraduate training, at Oberlin College, had been in mathematics (which didn't like me very much) and philosophy of science (which I liked a lot). This background undoubtedly colors my view of current bioanthropology and its future as I express it here. Genetics has been in full flower within anthropology for some time, but I think we have been conceptually constrained by historically driven attitudes that leave important things missing from anthropology, and even from biology in general. These attitudes have to do with the application of reductionism in genetics, and a consequent degree of removal from fundamental questions in Darwinian biology that ushered in this century, this should be remembered as we, in turn, usher in the next.

### REVISITING PHENOTYPES IN AN AGE OF GENOTYPES

How have living things become what they are, and what are the laws that govern their forms? W. Bateson (1894).

#### Some thoughts on the foundations of 20th century science

The 20th century inherited a view of Nature as an entity regulated by laws that were subject to discovery by science. Scientific respectability has required use of an axiomatic formalism based on mathematics or symbolic logic, influenced heavily by 19$^{th}$ century success in physics (e.g., Whitehead and Russell, 1910-13). Knowledge was to be

built from fundamental units, or atoms, which are understood by a set of basic postulates about them. This *Zeitgeist* underlies molecular reductionism in genetics, for example.

This has been a Darwinian century for biology. The initial postulate was Darwin and Wallace's "law" of evolution, that life derives from a common origin, screened by natural selection. The fundamental units are genes, which followed Mendelian "laws." Axiomatization of these 19th century elements occurred in the 30s and 40s as the "modern" or evolutionary synthesis: Life is genes; genes are life. Population genetics formalized the postulates, and evolution was defined as change in allele frequency, following laws involving the basic "forces" of mutation, selection, gene flow, and drift. Biology has its Central Dogma (one gene - one protein), and, like calculus, a Fundamental Theorem (Fisher, 1930). The modern synthesis essentially drove many topics from the mainstream of biology, including development, morphology, and perhaps even much of ecology (e.g., Gilbert et al., 1996). They were too soft.

The formalism of the modern synthesis provided legitimacy for the Darwinian approach, which was largely comparative and anatomical. Nevertheless, the linkage between formalism and application is a bit strange because it rested entirely on extrapolation from a few instances of directly observed short-term allele frequency examples unrelated to the traits of interest.

## Mid-century physical anthropology and genetics

My first real introduction to evolutionary thinking occurred in the middle 1960s when, as a professional meteorologist, I stumbled across W. W. Howell's (1959) engaging *Mankind in the Making*. He presented the origin and nature of humans, and of humans as primates, in the context of a deeply Darwinian perspective, that is, in terms of *post hoc* adaptive explanations of traits. When I returned to school in the late 60s, graduate students at Michigan were provided a devotedly, even devoutly, Darwinian view of life wholly based in the modern synthesis. We explained our major traits of interest, for example, upright posture or language ability, by confidently extrapolating from a few simple cases of allele frequency effects, such as sickle cell anemia and Rh maternal-fetal incompatibility. This was dubbed "modern physical anthropology" as early as 1950 in the subtitle of William Boyd's influential *Genetics and the Races of Man*.

By the late '60s, protein polymorphisms energized anthropological genetics by providing a wealth of taxonomic markers useful for reconstructing primate and human history (for entry to this literature see Cavalli-Sforza et al., 1992; Weiss, 1998; Harpending et al., 1998). Debates swirled about the origins of humans and particularly of anatomically modern humans, as could be inferred from gene frequencies. The two views now called the "Out of Africa" and "Multi-Regional" models are not new, and had long been at the core of the debate. Loring Brace used to remind us, in terms characteristically neither uncertain nor muted, of the previous century's history of myopic "catastrophists" versus wise men proffering a phyletic (Darwinian gradualistic) view. Then as now, most genetic analyses suggested a recent time of human origin, and then as now, the fossil record suggested a much earlier expansion from Africa. Then as now, there were potential confounders like gene flow (e.g., Weiss and Maruyama, 1976; Templeton, 1998). The issue is still not reconciled, and I think it is revealing of 20th century epistemology that the battle largely rests on genetic data, often stripped of serious consideration of the behavioral, demographic, morphological, or even paleontological implications of either scenario. They're too soft.

My interest has always been in phenotypes, broadly defined. As a graduate student, I was under the influence of Leslie White's idea of *culture* as a "superorganic" phenomenon, as well, perhaps implicitly, as the rage for group selection. So in my dissertation (Weiss, 1973) I tried to look, among other things, at how cultural evolution would be reflected in fitness-related demographic traits such as birth and death rates. Treating culture as a kind of biological super-phenotype now seems naive in

many ways, but if culture applies to groups and their relative success, it is still probably legitimate to ask what the connection between cultural and human biological evolution is, if any.

After a post-doctoral year studying Yanomama demography, I was privileged to be a faculty member within a fine population genetics group at the University of Texas medical center in Houston, where I had the luck to do a lot of anthropological work with Ranajit Chakraborty in particular. Technology improved dramatically as we entered the DNA age in the 80s. Because most of the resources were in medical schools, from thence came many pronouncements about human origins, and races — often by geneticists who were technologically aware but perhaps anthropologically challenged. Reconstructions based on elegant data often displayed little more than a pop-culture understanding of the evolutionary process, and this weakness still holds true. So, when an opportunity arose in 1985 to build a genetics program within the context of anthropology, I moved to head the Anthropology Department at Penn State. My thought was that those doing anthropological genetics should receive a daily tempering from colleagues savvy about human population processes, culture and prehistory. I hope we've had a salutary influence in helping establish modern genetics within anthropology facilities. Certainly, anthropological genetics is now more in flower than ever before, and more of it is done in anthropology departments. The biomedical world is discovering the importance of understanding human variation in studies of disease — a rude awakening for many. Anthropologists sit on policy-making panels. These are good trends. But as I noted at the outset, something important is still missing, and it has to do with phenotypes.

## A degree of removal

"Anthropological genetics" still mostly denotes the *timing* of historical events in our evolution, rather than their *cause*. Yet most biological anthropology is about complex phenotypes, many steps removed from single gene action. Our texts still rhetorically express evolutionary scenarios in modern-synthesis terms (e.g., mutations for language or brachiation arose by chance and were favored by selection, etc.), but actual genes are still rarely mentioned. I think we have lost sight of the ultimate question: How did we — the *organism* — get here? What role do genes play in that process? We seem largely oblivious to the dramatic developments in the broader world of genetics that deals directly with these functional questions. I think we should be part of that world.

It was only a few years ago that I realized how thoroughly we had been "synthesized" by our training and how insular my own reading had been. I had not realized the degree to which previous thought could be essentially silenced by being absent from our texts and hence our professional awareness (e.g., Mayr, 1982; Provine, 1971). An example of interest to me is William Bateson, who coined the term "genetics," but in his 1894 book raised serious questions about how gradual Darwinian evolution could explain the evolution of the kinds of discontinuous traits so important to 19$^{th}$ Century biologists: segmented, serially homologous traits. A hundred years later, the evolution of morphological traits is still explained in a way not easily reconciled except in a most generic sense with change in allele frequency.

I think biological anthropologists should be much better trained as general biologists, as some of our forebears had been when biology was simpler and more unified. I had not been a reader of the Drosophila or mouse literature, though I had heard of the Bithorax and Antennapedia genes, and knew vaguely of the homeobox genes responsible for these homeotic (segment identity changing) traits. These mutant phenotypes had in fact been known for decades and had been discussed in terms of their relevance to morphological evolution. Bateson coined the term and wrote his entire book on homeotic change. Our training should have made us as anthropologists aware of these issues, which largely involved the skeleton and dentition and were main concerns of leading biologists of the century, including Bateson, WK Gregory, and many others. My own epiphany occurred when, looking for a place to sit down, I chanced into a plenary session at an Amer-

ican Association of Human Genetics meeting in the late '80s at which Deborah Wolgemuth described a homologue of the Drosophila homeobox genes that had specific developmental function in the mouse (e.g., Wolgemuth et al., 1987). I scurried to the library and quickly learned of the extensive similarity of Hox gene expression in axial specification in vertebrates and invertebrates. Learning these things was a transforming experience for me that I tried to share in my luncheon talk at the 1990 AAPA meeting, about the importance of segmental organization (Weiss, 1990).

Bob Ferrell and I had for years discussed how one might apply modern genetics to bear on an understanding of segmental traits, like the evolution of the dentition from a homodont to heterodont condition. These changes occurred along a linear anatomical axis, in a way highly similar to the evolution of the vertebral column and limb, structures that had been found to be regulated at least in part by the homeobox genes. It seemed to me that the evolution and basic biology of the dentition could finally be attacked with real genetic methods. I spent a sabbatical in 1992 with Frank Ruddle at Yale, to learn developmental molecular genetic methods, thinking (wrongly, it now appears) that the dentition would be an easy hit as but another Hox-regulated system. Since then I have worked on the problem of dental patterning (e.g., Weiss et al., 1998), using various developmental and genomic approaches in a variety of animal model systems, in collaboration with various other friends and colleagues.

Almost any complex trait can now be studied by an armament of methods largely being provided by the massive current investment in biomedical genetics. The traits are challenging and will not yield a rapid or simple genetic solution. But they are important traits of biology, and of human evolution, and there is no reason to shy away from difficult problems if our goal is to understand life. I hope a few determined and forward-looking anthropology departments and their students will be stimulated to enter this competitive, expensive, and daunting — but exciting and important — field. It will require determination, and will not look very "anthropological" at first, but questions about complex traits are our traditional questions. I believe this work should retain a connection to the cultural and historical sides of anthropology. If we do not do this, then as happened with genetic studies of human variation (and race), we risk complaining from the sidelines about what others, with scant understanding of evolution are saying about our subject (e.g., see Smith and Schneider, 1998).

## But — what about genes generally?

Having said this, I am not a blind apologist for genetics, and I believe even deeper issues need examination. Technology permits progress on the kinds of traits upon which Darwinian biology was based. But recent work in this area raises the question: What in fact *is* the role genes play in evolution?

Influenced by our theoretical underpinnings in the modern synthesis, we have tended to forget that natural selection screens phenotypes not genotypes: it is organisms that survive and reproduce. Darwin's pangenesis was a form of genetic determinism in which circulating heritable units (gemmules) were directly controlled by phenotypes. But genetic variation is not directly controlled by phenotypes (so far as we know), and DNA is not the only thing in an egg, bud, or spore. Though genes remain the only known quasi-permanent heritable material, what determines success is the phenotype of the organism. Selection does not identify the perfect genotype, and preserve it. Selection identifies phenotypes that are too imperfect and removes them. As we identify the genes involved in complex traits (most current data concern disease), we find that genetic reductionism does not work as well as we expected. The argument-by-design objection to evolution falls apart in a curious way. Complex traits result from millions of years of assembly through evolution by phenotypes, and are *not* put together as a good watchmaker would do it. Redundant, homeostatic, interlocking, and "noisy" mechanisms are involved.

Allele frequencies do change, must change, in evolution. But if evolution is basically a phenotypic process, what role do genes play in it? Nothing guarantees that individuals with the same phenotype must have the same genotype, and there are

many genetic ways to arrive at the same phenotypes (e.g., blood pressure). Nothing guarantees that a trait maintained in two species by natural selection since they shared a common ancestor must have the same genetic basis today. Over evolutionary time, there can be "phenogenetic" drift in the relationship between genotype and a given phenotype (Weiss and Fullerton, 2000). What is the relative importance, the "tempo and mode," of the evolutionary tracking between the two? If genes are one kind of theoretical atom, gene *interaction* may be a primitive element or "force" that must be added to the formal foundations of biology. A complex trait might better be viewed as a set of potentially changing interactions, constrained by selection, the trait itself ephemeral across generations — not your usual kind of "atom".

Nothing in these questions is specifically anthropological. But anthropologists, who have been deeply rooted in Darwinian thinking and concerned with complex phenotypes, may be particularly suited to study genes as entities that are part of, but not the entire rationale for, biology. Darwin's basic insight may last another century, or indeed, for the next millennium. But will genes remain the supreme object of our affections, or will we return to an interest in phenotypes as perhaps a more fundamental unit of life than the 20th century has allowed them to be? Let us at least ask the questions, and seek a modern rediscovery of Darwin's interest in the biology of phenotypes, after a most remarkable Darwinian century.

## ACKNOWLEDGMENTS

I thank Drs. Anne Buchanan and Emőke Szathmáry for their considerable and skillful editorial help.

## LITERATURE CITED

Bateson W. 1894. Materials for the study of variation, treated with special regard to discontinuity in the origin of the species. London:Macmillian. Reprinted with introduction by Webster G. 1992.Baltimore: Johns Hopkins University Press.

Boyd W. 1950. Genetics and the races of man: An introductioon to modern physical anthropology. Boston: Little, Brown.

Cavalli-Sforza L, Menozzi P, Piazza A. 1992. History and geography of human genes. Princeton: Princeton University Press.

Fisher R 1930. The genetical theory of natural selection. Oxford: Clarendon Press.

Gilbert SF, Opitz JM, Raff RA.1996. Resynthesizing evolutionary and developmental biology. Dev Biol 173:357;372.

Harpending H, Batzer MA, Gurven M, Jorde LB, Rogers AR, Sherry ST.1998. Genetic traces of ancient demography. PNAS 95:1961-1967.

Howells WW.1959.Mankind in the makiing. Garden City, NY: Doubleday.

Mayr E. 1982. The growth of biological thought. Cambridge, MA: Harvard Press.

Smith K, Schneider R. 1998. Have gene knockouts caused evolutionary reversals in the mammalian first arch? Bioessays. 1998, 20:245-255.

Templeton A. 1998. Human races: a genetic and evolutionary perspective. Am Anthropol 100:632-650.

Weiss KM. 1973.Demographic models for anthropology. Memoir No. 27. Washington, DC: Society for American Archeology.

Weiss KM, Maruyama T. 1976.. Archeology, population genetics, and studies of human racial ancestry. Am J Phys Anthropol 44:31-49.

Weiss KM. 1990. Duplication with variation: metameric logic in evolution from genes to morphology. Ybk Phys Anthropol 33:1-23.

Weiss KM. 1998. Coming to terms with human variation. Ann Rev Anthropol 27: 273-300.

Weiss K, Zhao Z, Stock D. 1998. Dynamic interactions and dental patterning. Cr Rev Oral Biol and Med 9:369-398.

Weiss KM, Fullerton SM. 2000. Phenogenetic drift and the evolution of genotype-phenotype relationships. Theor Pop Biol, in press.

Whitehead AN, Russell B. 1910-13.Principia mathematics. Cambridge: Cambridge University Press.

Wolgemuth DJ, Viviano CM, Gizang-Ginsberg E, Frohman MA, Joyner AL, Martin GR. 1987. Differential expression of the mouse homeobox-containing gene Hox-1.4 during male germ cell differentiation and embryonic development. Proc Natl Acad Sci USA 84: 5813-5817.